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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,242	CANTLEY ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,17,21,22,31,36,40,71 and 72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,17,21,22,31,36,40,71 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 March 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are pending in the application.

[2] Applicant's amendment to the claims, filed on 3/23/09, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

Election/Restriction

[3] Applicant's election of species phenformin in the reply filed on 3/23/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

[4] The claims are being examined only to the extent the claims read on the elected species. Election was made without traverse in the reply filed on 3/23/09.

Claim to Priority

[5] The instant application is filed under 35 U.S.C. 371 as a national stage filing of PCT/US04/29437, filed on 9/4/04, which claims domestic priority under 35 U.S.C. 119(e) to US provisional applications 60/501,513, filed on 9/9/03, and 60/506,705, filed on 9/26/03.

Information Disclosure Statement

[6] All references cited in the IDS filed on 6/19/07 have been considered by the examiner. A copy of Form PTO/SB/08 is attached to the instant Office action.

[7] If the examiner has inadvertently overlooked an IDS in the application file, applicant is kindly requested to alert the examiner to this oversight in the response to this Office action.

Oath/Declaration

[8] The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either an application data sheet or supplemental oath or declaration.

Specification/Informalities

[9] The specification is objected to as the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: ---Method for Treating Cancer by Increasing AMP Kinase Activity---.

[10] The listing of references in the specification at pp. 38-41 and 52-60 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP

§ 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

[11] The drawings are objected to as describing Figures 5a, 5b, and 5c (specification at p. 7, top), however, there is only a Figure 5 in the drawing figures, *i.e.,* there are no parts a, b, and c of Figure 5. Appropriate correction is required.

Claim Objection

[12] Claim(s) 12, 21, 31, 40, and 71-72 are objected to in the recitation of "LKB1". Abbreviations, unless otherwise obvious and/or commonly used in the art, *e.g.,* "DNA", should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

[13] Claims 12 and 22 are objected to in the recitation of "(cells of)" and "(cells)", respectively. In order to improve claim form, it is suggested that, *e.g.,* the parentheses be removed from the above noted terms.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[14] Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] The term “reduced…LKB1 activity” in claims 12 (claims 17 and 21-22 dependent therefrom), 31 (claims 36 and 40 dependent therefrom), 71, and 72 is unclear absent a statement defining to what the activity is being compared. The term “reduced…LKB1 activity” is a relative term and the claims should define and clearly state as to what the activity is being compared. In the absence of such a reference for comparison, the scope of cancers “characterized by reduced…LKB1 activity” is unclear.

[b] Claims 12 (claims 17 and 21-22 dependent therefrom) and 31 (claims 36 and 40 dependent therefrom) are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. In order to achieve the desired outcome of the claimed methods, *i.e.,* “treating cancer” or "promoting apoptosis" by administering a compound that increases AMPK activity, it would appear that the cell must express AMPK in order to achieve promoting apoptosis. In the absence of AMPK, it is unclear as to how a skilled artisan is to achieve promoting apoptosis with a compound that activates AMPK.

[c] Claims 21 and 40 recites the limitation "the mutation". There is insufficient antecedent basis for this limitation in the claim and it is suggested that the noted phrase be amended to recite, *e.g.,* "a mutation".

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[15] Claims 12, 17, 21-22, 31, 36, and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In providing guidance for evaluating a claimed invention for adequate written description, MPEP 2163.II.A.1 states, "the examiner should determine what the claim as a whole covers. "Claim construction is an essential part of the examination process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997)."

Claim 12 (claims 21-22 dependent therefrom) is drawn to a method for treating cancer by administering to a subject having a cancer characterized by reduced or absent LKB1 activity an effective amount of a genus of compounds that increases AMPK activity in the cells of the subject. Claim 31 (claim 40 dependent therefrom) is drawn to a method for promoting apoptosis of cells having reduced or absent LKB1 activity by contacting the cells with a genus of compounds that activates AMPK. The structure of the compound of claims 12 and 31 is undefined and unlimited in claims 12 and 31. While claims 17 and 36 recite "wherein the compound is metformin or an analog

or derivative thereof", the structure of the "analog or derivative" of metformin is undefined and unlimited.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Sufficient description to show possession of such a genus "may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In this case, the genus of compounds encompasses *any* compound that increases or activates AMPK activity. The species encompassed by the genus are widely variant with respect to both structure and function, including, *e.g.,* small molecule organic compounds, peptides, polypeptides, antibodies, and nucleic acids. While the specification discloses certain species of compounds that are encompassed by the genus (*e.g.,* p. 11, lines 1-10), there is no substantial shared structural feature among these species. Here, the disclosed representative species fail to describe all members of the recited genus of compounds. Given the lack of description of a representative number of compounds, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[16] Claim(s) 12, 17, 21-22, 31, 36, and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a cancer or a method for promoting apoptosis using the compounds set forth in the specification at p. 11, lines 1-10, does not reasonably provide enablement for using any compound that increases or activates AMPK activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are

summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors considered to be most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: The claims are so broad as to encompass methods using *any* compound that increases or activates AMPK activity, wherein the compound has *any* structure, including any small organic compound, any peptide, any polypeptide, any antibody, and any nucleic acid, so long as it increases or activates AMPK activity. It should be noted that the target of the compound is not limited to AMPK and the compound can increase or activate AMPK activity either directly or indirectly by altering the activities of, *e.g.,* transcription factors that enhance AMPK expression directly or indirectly.

The nature of the invention: According to the specification at p. 2, lines 19-27, "It has now been discovered that the LKB1 protein directly phosphorylates AMP kinase…and activates its kinase activity…LKB1 is the major AMPK kinase in mammalian cells and suggest a unexpected connection between the response of cells to metabolic stress and tumorigenesis".

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: At the time of the invention, the prior art recognized that LKB1 is a tumor suppressor (see, *e.g.,* Shen et al., *Clin. Cancer Res.* 8:2085-2090, 2002); the prior art recognized that LKB1 phosphorylates AMPK (see, *e.g.,* Carling et al., US Patent Application Publication 2005/0026233 A1; cited in the IDS filed on 6/19/07); the prior art recognized that metformin activates AMPK (see, *e.g.,* Zhou et al., *J. Clin. Invest.* 108:1167-1174, 2001); and the prior art recognized that phenformin is useful in the treatment of cancer (see, *e.g.,* Dilman et al., *Gerontology* 26:241-246, 1980).

The amount of direction provided by the inventor; The existence of working examples: As previously noted, the specification discloses certain working examples of compounds that are asserted to be useful within the claimed method. Also, a skilled artisan could identify those compounds that *directly* affect AMPK activity by measuring AMPK activity in the presence and absence of the compound. However, the claims are not limited to those compounds that directly increase or activate AMPK activity, and broadly encompass compounds that *indirectly* increase or activate AMPK activity. However, the specification fails to provide any specific guidance regarding such compounds and/or assays for identifying such compounds.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of screening for compounds that increase or activate AMPK activity were known in the art at the time of the invention, it was not routine to identify *all* compounds having any structure that increase or activate AMPK either by direct or indirect effect. Such experimentation was not routine.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the significant amount of non-routine experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. As such, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[17] Claim(s) 31 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Shen et al. (*Clin. Cancer Res.* 8:2085-2090, 2002; hereafter referred to as "Shen").

CLAIM INTERPRETATION: According to the specification, a compound that activates AMPK encompasses agents that increase expression of LKB1, including introducing one or more copies of the LKB1 gene (p. 11, lines 10-12).

The reference of Shen teaches the cell line MDA-MB-435 lacks the *LKB1* gene (p. 2085, column 2, bottom) and teaches transfection with an expression vector encoding LKB1 polypeptide (p. 2085, column 2, bottom). This anticipates claims 31 and 40 as written.

Claim Rejections - 35 USC § 102/103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[18] Claim(s) 12, 17, 21, 31, 36, 40, and 71-72 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Dilman et al. (*Arch Geschwulstforsch* 48:1-8, 1978; "hereafter referred to as "Dilman1") OR Dilman et al. (*Gerontology* 26:241-246, 1980; hereafter referred to as "Dilman2") as evidenced by Shen (*supra*) and Zhang et al. (*Am. J. Physiol. Circ. Physiol.* 293:H457-H466, 2007; hereafter referred to as "Zhang"). See MPEP 2112.III regarding a rejection under 35 U.S.C. 102/103. See also 2131.01.III regarding a multiple reference 35 U.S.C. 102 rejection.

CLAIM INTERPRETATION: Claims 12 and 71 recite "administering to a subject", where the specification defines the term "subject" as encompassing a "rodent" (p. 15, lines 1-2). Claims 12 and 71 also recite "a cancer characterized by reduced or absent LKB1 activity", which has been interpreted as encompassing cancer of the mammary glands in view of the teachings of evidentiary reference Shen, cited in accordance with MPEP 2131.01.III. Evidentiary reference Shen teaches LKB1 "plays a role in tumor suppressor function in human breast cancer" (p. 2090, column 1); teaches reduced expression of LKB1 in human breast cancer cell lines (p. 2085, column 2, middle; paragraph bridging pp. 2086-2087); and teaches LKB1 expression is correlated with shorter survival, *i.e.,* lower *LKB1* expression, shorter survival (p. 2090, column 1 and p. 2089, Figure 6). Claims 12 and 17 also require administering "an effective amount" of a compound that increases AMPK activity. According to the specification, an "effective amount" encompasses an amount that is effective in "slowing or reversing the progression of cancer" (p. 21, lines 7-10).

The reference of Dilman1 teaches inhibition of DMBA-induced carcinogenesis in the mammary gland of rats by administering phenformin (p. 1, abstract). Evidentiary reference Zhang teaches phenformin activates AMPK and increases AMPK activity (p. H457, abstract and p. H465, column 1). Since LKB1 expression is reduced in breast cancer as evidenced by Shen, the rats of Dilman1 have mammary cancer, phenformin activates AMPK and increases AMPK activity as evidenced by Zhang, and phenformin results in a "slowing or reversing the progression of cancer" in the rats of Dilman1, this anticipates claims 12, 17, 21, 31, 36, 40, and 71-72.

The reference of Dilman2 teaches phenformin produced a significant reduction in tumor incidence and prolonged life span in mice with mammary tumors (p. 241, abstract and p. 244, column 1). According to Dilman2, phenformin treatment “not only cut down the incidence of mammary tumours but also all other types of neoplasms (sentence bridging columns 1-2). Evidentiary reference Zhang teaches phenformin activates AMPK and increases AMPK activity (p. H457, abstract and p. H465, column 1). Since LKB1 expression is reduced in breast cancer as evidenced by Shen, the mice of Dilman2 have mammary cancer, phenformin activates AMPK and increases AMPK activity as evidenced by Zhang, and phenformin results in a “slowing or reversing the progression of cancer” in the mice of Dilman2, this anticipates claims 12, 17, 21, 31, 36, 40, and 71-72.

The evidence of record supports the examiner’s position that mammary cancer is encompassed by a “cancer characterized by reduced or absent LKB1 activity”, wherein the cancer comprises cells that have “reduced or absent LKB1 activity”. Since the Office does not have the facilities for determining whether or not the rodents of the Dilman references have a cancer "characterized by reduced or absent LKB1 activity”, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[19] Claim(s) 22 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Dilman1 OR Dilman2 as evidenced

by Shen and Zhang and as further evidenced by Caraci et al. (*Life Sci.* 74:643-650, 2003; hereafter referred to as "Caraci").

The relevant teachings of the references of Dilman1 and Dilman2 and evidentiary references Shen and Zhang are set forth above. Evidentiary reference Caraci teaches that phenformin induces apoptosis of cancer cell lines (*e.g.,* p. 649, middle). Thus, the method of Dilman1 or Dilman2, in addition to increasing AMPK activity as evidenced by Zhang, also subjects the cancer cells to a cell death stimulus as evidenced by Caraci. This anticipates claim 22.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[17] Claim(s) 12, 17, 21-22, 31, 36, 40, and 71-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Dilman1, Dilman2, and Dilman et al. (*Cancer Lett.* 7:357-361, 1979; hereafter referred to as "Dilman3") as evidenced by Shen, Zhang, and Caraci.

The claims are drawn to methods as noted above.

Teachings of Dilman1 and Dilman2 are set forth above. Teachings of the evidentiary references Shen, Zhang, and Caraci.

Dilman1 further teaches that the positive effects of phenformin on cancer in rats suggests that such studies should be conducted in man (p. 7, middle). Dilman2 further teaches that phenformin “not only cut down the incidence of mammary tumours but also all other types of neoplasms, leukemia included" (p. 244, sentence bridging columns 1-2).

Dilman3 teaches that phenformin itself “inhibited growth of sarcoma-180, tumor of the cervix uteri and Walker 256 carcinoma" and “distinctly suppressed hepatoma-22a…and Lewis lung tumor” (p. 359) and further teaches that phenformin positively potentiates the antitumor effect of two anti-cancer therapies (p. 357, abstract). According to Dilman3, the disclosed results “confirm the conclusion…that it is desirable to explore the possibility of improving the results of the chemotherapy of tumor patients by giving them a simultaneous course of phenformin” (p. 360).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Dilman1, Dilman2, and Dilman3 to treat any cancer with phenformin, optionally in combination with another chemotherapy, including those cancers that are “characterized by reduced or absent LKB1 activity”. One would have been motivated to do this because of the teachings of the beneficial effects of phenformin on life span and tumor incidence as taught by Dilman1, Dilman2, and Dilman3 and the express teachings of treating cancer in human patients with phenformin as taught by Dilman2 and Dilman3. One would have had a reasonable expectation of success for administering or co-administering phenformin to a subject with any cancer, including those cancers that are “characterized by reduced or absent

LKB1 activity" because of the results of Dilman1, Dilman2, and Dilman3. Therefore, claims 12, 17, 21-22, 31, 36, 40, and 71-72, drawn to methods as described above, would have been obvious to one of ordinary skill in the art at the time of the invention.

Citation of Relevant Prior Art

[20] The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: 1) Anisimov, Ann. NY Acad. Sci 621:373-384, 1991 and 2) Dilman, Ann. NY Acad. Sci. 621:385-400, 1991.

Conclusion

[21] Status of the claims:

- Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are pending.
- Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656